BETH ISRAEL DEACONESS MEDICAL CENTER
A member of CAREGROUP
Charles Poser, M.D., FRCP
Visiting Professor of Neurology
Senior Neurologist

A major teaching hospital of Harvard Medical School

Michael Roberts Esq
GRAYDON HEAD RITCHEY
P.O.Box 6464
Cincinnati OH 45201-6464

re: Eric Jeffries

Dear Mr. Roberts:

At your request I have reviewed two letters from Dr. Burton Zweiman dated respectively April 24 and October 5, 2001, a copy of his CV and a series of 20 reprints of published articles. In addition, I have reviewed additional material in my possession, some of which I have appended to this report.

The medical information available to me was contained in Dr. Zweiman's April letter, in addition to some notes from Dr. Byron Hyde who had referred Mr. Jeffries to me for consultation. I note the following as being relevant: Mr. Jeffries received a Hep B and Hep A vaccine on June 18, 1997. Nine days later he reported joint pains, nightsweats, headache, decreased energy and his "usual" abdominal pain. He also complained of numbness in hands and feet. It is not until September 1998 that he started suffering from prominent fatigue, searing muscle pain, pain in his knees and elbows, "nerve pain in back of the eyes". He also complained of other problems including cognitive dysfunction [I think that this is quite significant in view of the fact that Mr. Jeffries is an investment banker]. These symptoms have persisted with what sounds like fluctuations in severity.

Dr Zweiman's opinion can be divided into two parts: the first relates to the nature of Mr. Jeffries' illness, the second to the relationship between his symptoms and the hepatitis vaccination. I will address these in the same order.

THE NATURE OF THE ILLNESS

I saw Mr. Jeffries in consultation in June 2000. I do not believe that he was ever seen by Dr. Zweiman. Based on the available medical history and my own examination, I believe that Mr. Jeffries

Department of Neurology
330 Brookline Avenue
Boston, MA 02215

617-667-2063 phone
617-667-5216 fax
cposer@caregroup.harvard.edu

suffers from the chronic fatigue syndrome, also known as myalgic encephalomyelitis, a term coined by Professor Peter Behan of the University of Glasgow, a world expert on this disease. The complex is often referred to as CFS/ME and I will do so in this report. The same diagnosis of CFS/ME was made by Dr. Byron Hyde of Ottawa, Canada who is also a recognized expert in this disease. I have seen several dozen patients with CFS/ME and have, in fact, published a set of diagnostic criteria that are much more stringent than the ones promulgated by the CDC and NIH which are in current use (see attachment 1). I find it remarkable that Dr. Zweiman does not include CFS/ME in his differential diagnosis, suggesting his lack of familiarity with this well recognized syndrome. I am unable to determine from his CV if Dr. Zweiman actually sees neurological patients since there is no evidence that he ever had training in neurology. I have also appended a recent review of CFS/ME by Levine, Jacobson and Peterson (Attachment 2).

The exact nature of CFS/ME remains a matter of some controversy despite the growing body of literature on the subject. In part this is due, in my opinion, to the extremely broad CDC and NIH criteria, in part due to the overlap with other syndromes known as fibromyalgia and myofasciitis. This overlap is discussed in the Levine et al. paper.

The reason that I prefer the term myalgic encephalomyelitis is that I believe, as does Prof. Behan, that the syndrome represents the late, long term sequelae of a postinfectious or postvaccinal encephalomyelitis. In other words, the patient's symptoms are the manifestations of damage done to the nervous and other organ systems at the time of the acute episode. It is therefore not surprising that no changes can be found in the immune system when the CFS/ME is fully established. Definite evidence of nervous system damage has been repeatedly demonstrated in some patients with CFS/ME including white matter lesions on MRI which are indistinguishable from those of multiple sclerosis (Attachment 1).

I am surprised that Dr. Zweiman so casually dismisses Mr. Jeffries' unequivocal classic episode of serum sickness starting nine days after the vaccine injection.

THE RELATIONSHIP WITH THE VACCINE

All vaccines can and do on rare occasions, cause neurological problems. In fact, there is an exact experimental model for postinfectious and postvaccinal encephalomyelitis, called experimental allergic encephalomyelitis. It is curious that studies of the deleterious side effects of vaccines almost never refer to this kind of evidence. I should also point out that vaccines are complex mixtures containing more than one antigen. This was well stated by Isacson and Stone: "There is a multiplicity of antigens in any given viral vaccine preparation:(a) those associated with the virus, either as part of the virion or non-structural proteins, interferons, etc. induced by the virus;(b) those of the host cell, either existing separately or attached to the virion, including host cell antigens whose a..genic specificity has been altered by

viral action;(c) those of the surrounding media, including nutrients and antibiotics; and (d) those derived from material or equipment used for purification and those which may be added to stabilize the final product" (Isacson P, Stone A. Allergic reactions associated with viral vaccines. Progr Med Virol 1971; 13: 239-270). The purpose of vaccination is to induce the production of antibodies against a particular organism (e.g. virus). Therefore the immunological challenge is the same for a vaccine as for the virus against which it is prepared.

Adverse reactions are, fortunately, quite rare and indeed rarely if ever reach the "statistically significant" 5% level. Thus, the documentation provided by Dr. Zweiman capitalizes on that fact and uses it to deny the possibility of an association between the vaccine and the CFS/ME syndrome.

For the past several years, medical science and practice have been subjected to what I call the tyranny of statistical significance. The 5% significance is nothing more than a convention yet has assumed the status of a natural law! Epidemiological studies are also deceptive because they assume that all individuals share the same genetic and immunological background, a grossly inaccurate and naive assessment. The fallacy of using statistical analysis to deny a causal association is illustrated by a series of statements by experienced and knowledgeable statisticians attached to this report (Attachment 3).

Neurological complications of hepatitis vaccine have been reported by a number of authors, but are dismissed as being anecdotal, a rather curious practice when one considers that medical knowledge has been built on such anecdotal evidence, the medical equivalent of the legal profession's precedent and case citations! Public health considerations clearly outweigh concerns about rare, individual untoward side effects. Great emphasis is placed on the safety of vaccines and, indeed on the extreme rarity of complications. As a result, underreporting of such adverse effects ensues making rare events even rarer. In my own experience, a preceding vaccination is rarely mentioned spontaneously by patients.

Even when neurologic complications are reported, they are dismissed as not being of epidemiological significance. A good example of such practice is the initial report on postmarketing surveillance for neurologic adverse reactions after hepatitis B vaccination by Shaw et al. (The summary is attachment 4). Note the following: "In some analyses, Guillain-Barre syndrome was reported significantly more often than expected. However, no conclusive epidemiologic association could be made between any neurologic adverse event and the vaccine. [And here comes the mantra!] Even if such association did exist, the preventive benefits of the vaccine in persons at high risk for hepatitis B would unequivocally outweigh the risk of any neurologic adverse effect."

The response to the immunologic challenge of a vaccination is totally individual and therefore unpredictable. It depends on the

person's genetic make up and prior immunologic history. The fact that different parts of the nervous system are affected by the same vaccine in different individuals is a reflection of the variability in the vulnerability of the nervous system which is also related to genetic and immunologic factors. This was experimentally demonstrated by Kadlubowski and Hughes. (see summary in attachment 5).

Finally, I should like to mention a very recent article, published in the world's most prestigious neurological journal, Brain, which describes 50 patients with macrophagic myofasciitis, a variant of CFS, all of whom had been vaccinated against hepatitis B or A, or had received tetanus toxoid. The authors ascribe the reaction to the aluminum hydroxide contained in the vaccines. (Attachment 6)

CONCLUSION

I am of the opinion that Mr. Jeffries suffers from the chronic fatigue syndrome/myalgic encephalomyelitis, and, to a reasonable degree of certainty. that it is the long term result of his having been vaccinated against hepatitis A and B in June 1997.

I am licensed to practice medicine in the Commonwealth of Massachusetts. I was certified in neurology in 1957. For over 40 years, I have specialized in demyelinating diseases incluing the neurological complications of vaccinations. A copy of my CV is enclosed. (attachment 7)

Very sincerely,

Charles M. Poser

July 28, 2000

Dr. Byron Hyde
121 Iona Street
Ottawa K1Y 3MI
Canada

re: Eric Jeffries

Dear Dr. Hyde:

Mr. Jeffries was seen on June 7, 2000 at your request. He states that he received injections of recombinant vaccine against hepatitis A and B in June 1997. About one week later, he started exeriencing a constellation of symptoms including severe , incapacitating fatigue, abdominal cramps, joint and muscle pains, profuse sweating and recurrent numbness of the right arm and leg. He has also noted memory problems and difficulty sleeping.

About one year prior to vaccinations he had aphthous ulcers of the mouth and trunk. He is known to be allergic to sulfa drugs.

His neurological examination was essentially within normal limits.

I have also received the results of a SPECT scan which revealed a pattern consistent with changes seen in chronic fatigue syndrome, a marked increase of antimicrosomal antibodies, an increase of CD4/CD8 cell ratio, and a thyroid biopsy showing papillary carcinoma.

OPINION

Mr. Jeffries gives what I consider to be the classical history of chronic fatigue syndrome (CFS). He fulfills my own diagnostic criteria for CFS which are much more stringent than those proposed by the Center for Disease Control (1). The temporal relationship to the vaccination with recombinant hepatitis A and B vaccine is such as to strongly suggest a causal relationship. Indeed, I have seen several cases of classical CFS immediately following, and almost certainly resulting, from such vaccination. I am impressed by the results of the SPECT and PET scans and by the changes in his immune system. I do not believe that the thyroid carcinoma is related to this condition. In this case, I would suggest that the alternative appellation of the CFS, i.e. chronic myalgic encephalomyelitis is more appropriate in view of the changes just mentioned.

The prognosis for patients affected with this condition is very guarded. Men, in my experience, do worse than women with this syndrome. The prospects for recovery and return to gainful employment are quite dismal.

I want to thank you for referring this interesting patient to me.

Very sincerely,

Charles M. Poser

1. Poser CM Myalgic encephalomyelitis/chronic fatigue syndrome and multiple sclerosis: differential diagnosis. EOSJ Immunol Immunopharmacol 1995; 15: 50-52.

BETH ISRAEL DEACONESS MEDICAL CENTER
BOSTON, MA 02215

Eric Jeffries
146 1024.
[illegible]

Date	Patient Notes	Addressograph

6/7/00 Hepatitis A & B June 1997
1 week later severe headache - pains through his body - sweat profusely, numbness R arm & leg early on -
now his ability go to sleep and waking him up [illegible] sleep.
Has sense of well being -
Also severe fatigue.
Stopped working in Sept. 1998

Severe muscle pain, joint pains, memory problem, sleep problem - allergic to sulfa drugs

~~Has~~ Treated with Prednisone 40mg for 2 mo. - it helped the fatigue

Dx classical chronic fatigue syndrome.

Amantadine 100mg bid
Neurontin 400 tid

See attached notes

[signature]

MR 001055

MC0221 4/98

Telephone

Date

02/1/01 Football injury 20 yrs affecting neck

513-871-8599

→ MRI of C-spine + Neurotense protocol

[illegible signature]